



## N THE UNITED STATES PATENT AND TRADEMARK OFFICE Group Art Unit 1639

Patent Application of

David Edwin Thurston, et al.

Application No. 10/602,521

Confirmation No.: 2183

Filed: June 24, 2003

Examiner: Epperson, Jon D.

"COLLECTION OF COMPOUNDS"

I, Heather M. McGowen, hereby certify that this correspondence is being deposited with the US Postal Service as first class mail in an envelope addressed to Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on the date of my signature.

Mostherm. Mc Dave

Signature

March 8, 2005

Date of Signature

SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT PURSUANT TO 37 CFR §1.97(b)

Mail Stop Amendment Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Sir:

The Examiner's attention is directed to the references which are listed on the attached Form PTO/SB/08A and PTO/SB/08B and copies of non-U.S. patent references are attached.

Also, the Examiner's attention is directed to:

Examiner's Initials

1. U.S. Patent Application Serial No. 09/763,767, filed 2/26/2001.

2. U.S. Patent Application Serial No. 10/824,743, filed 4/15/2004.

Applicants request that the Examiner initial the above once considered.

Citation of these references is respectfully requested.

No concession is made that these documents are prior art, and Applicant expressly reserves the right to antedate the documents as may be appropriate.

Respectfully submitted,

Charlene L. Yager Reg. No. 48,887

File No. 065435-9027

Michael Best & Friedrich LLP One South Pinckney Street P. O. Box 1806 Madison, WI 53701-1806 (608) 257-3501

Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE persons are required to respond to a collection of information unless it contains a valid OMB control number.

Substitute for form 1449/PTO

INFORMATION DESCLOSURE
STATEMENT BY APPLIE ANT

(use as many sheets as necessary)

Sheet

	Complete if Known	
Application Number	10/602,521	
Filing Date	June 24, 2003	
First Named Inventor	David Edwin Thurston	
Group Art Unit	1639	-
Examiner Name	Epperson, Jon D.	
Attorney Docket Number	065435-9027	-

	U.S.	PATENT DOCUMENTS		
Examiner Initials	U.S. Patent Document Number	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document	
	4,185,016	Takanabe et al.	1/22/1980	
"	5,143,854	Pirrung et al.	9/1/1992	
	6,747,144	Thurston et al.	6/8/2004	
	6,562,806	Thurston et al.	5/13/2003	
	6,608,192	Thurston et al.	8/19/2003	
	2003-0120069	Thurston et al.	6/26/2003	
	2003-0195196	Thurston et al.	10/16/2003	

		]	FOREIGN PATENT DOCUME	NTS		
Examiner Initials	Country Code	Foreign Patent Document Number	Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document	Translation	English Abstract
	wo	88/07378	Cancer Research Campaign Technology Ltd.	10/6/1988		
	wo	89/10140	Cancer Research Campaign Technology Ltd.	11/2/1989		_
	wo	93/08288	Cancer Research Campaign Technology Ltd.	4/29/1993		
	wo	93/18045	Cancer Research Campaign Technology Ltd.	9/16/1993		
	wo	00/12506	The University of Portsmouth Higher Education Corp.	3/9/2000		
	wo	00/12507	The University of Portsmouth Higher Education Corp.	3/9/2000		
	EP	0239400A2	Winter, G.P.	9/30/1987		
	FR	2027356	Fujisawa Pharmaceutical Co. Ltd.	12/29/1969		
	JP	53-82792	Microbiological Chemical Research	7/21/1978		

Examiner	Date	
Signature	Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Burden Hour Statement: This form is estimated to take 2.0 hours to complete. Time will vary depending upon the needs of the individual case. Any comments on the amount of time you are required to complete this form should be sent to the Chief Information Officer. Patent and Trademark Office, Washington, DC 0231.

DO NOT SEND FEES OR COMPLETED FORMS TO THIS ADDRESS. SEND TO: Commissioner for Patents, P.O. Box Alexandria, VA 22313-1450.

Substitute for fi	orm 1449B/PTO			Complete if Known		
Substitute for form 1447B/1 TO				Application Number	10/602,521	
<b>INFOR</b>	MATION	N DISCL	OSURE	Filing Date	June 24, 2003	
STATEMENT BY APPLICANT				First Named Inventor	David Edwin Thurston	
				Group Art Unit	1639	
(use as many sheets as necessary)			)	Examiner Name	Epperson, Jon D.	
Sheet	i	of	6	Attorney Docket Number	065435-9027	

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS
Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, pages(s), volume-issue numbers(s), publisher, city and/or country where published.
ALBERICIO, F. et al., "NPE-Resin, A New Approach to the Solid-Phase Synthesis of Protected Peptides and Oligonucleotides II. Synthesis of Protected Peptides <sup>1,2</sup> ," <i>Tetrahedron Letters</i> , 32:1515-1518 (1991)
ALBERICIO, F. et al., "NPE-resin, a new approach to the solid-phase synthesis of protected peptides and oligonucleotides," <i>Peptides</i> 1990, Proc. 21.sub.st Eur. Pept. Symp., 134-136 (1990)
BAGSHAWE et al., "Antibody-Enzyme Conjugates Can Generate Cytotoxic Drugs from Inactive Precursors at Tumor Sites," Antibody, Immunoconjugates, and Radiopharmaceuticals, 4, 915-922 (1991)
BARALDI, P.G. et al., "Synthesis, in Vitro Antiproliferative Activity, and DNA-Binding Properties of Hybrid Molecules Containing Pyrrolo[2,1-c][1,4]benzodiazepine and Minor-Groove-Binding Oligopyrrole Carriers," J. Med. Chem., 42, 5131-5141 (1999)
BAYLEY, H. et al., "Photoactivatable drugs," TIPS, 8, 138-143 (1987)
BERRY, J. M. et al., "Solid-phase synthesis of DNA-interactive pyrrolo[2,1-c][1,4]benzodiazepines," Tetrahedron Letters, 41, 6171-6174 (2000)
BRIDGES, R.J. et al., "Conformationally Defined Neurotransmitter Analogues. Selective Inhibition of Glutamate Uptake by One Pyrrolidine-2,4-dicarboxylate Diastereomer," J. Med. Chem., 34, 717-725 (1991)
BUNDGAARD, H., "Design and Application of Prodrugs," A Textbook of Drug Design and Development, eds Krogsgaard-Lassen, P., and Bundgaard, H., Harwood Academic Press, 113-135 (1991)
CARRUTH, J.A.S., "Clinical applications for photodynamic therapy," J. Photochem Photobiol., 9, 396-397 (1991)

Examiner	Date	
Signature	Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute for form 1449B/PTO				Complete if Known		
Sabsinate ioi i	0111111111111111			Application Number	10/602,521	
<b>INFOR</b>	<b>MATIO</b> I	N DISCL	OSURE	Filing Date	June 24, 2003	
STATEMENT BY APPLICANT				First Named Inventor	David Edwin Thurston	
				Group Art Unit	1639	
	(use as many she	eets as necessary	)	Examiner Name	Epperson, Jon D.	
Sheet	2	of	6	Attorney Docket Number	065435-9027	

	OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS
Examiner Initials	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, pages(s), volume-issue numbers(s), publisher, city and/or country where published.
	CULVER et al., "In Vivo Gene Transfer with Retroviral Vector-Producer Cells for Treatment of Experimental Brain Tumors," Science, 256, 1550-1552 (1992)
	DALTON, S. and TREISMAN, R, "Characterization of SAP-1, a Protein Recruited by Serum Response Factor to the c-fos Serum Response Element," Cell, 68, 597-612 (1992)
	DANGLES, O. et al., "Selective Cleavage of the Allyl and Allyloxycarbonyl Groups through Palladium-Catalyzed Hydrostannolysis with Tributyltin Hydride. Application to the Selective Protection-Deprotection of Amino Acid Derivatives and in Peptide Synthesis," J. Org. Chem., 52, 4984-4993 (1987)
	DRESSMAN, B.A., et al., "Solid Phase Synthesis of Hydantoins Using a Carbamate Linker and a Novel Cyclization/Cleavage Step," <i>Tetrahedron Letters</i> , 37, 937-940 (1996)
	EASHOO, M. et al., "Fibers from a Low Dielectric Constant Fluorinated Polyimide: Solution Spinning and Morphology Control," J. Polymer Science, 35:173-185 (1997)
	ENGLEHARDT et al., "Direct gene transfer of human CFTR into human bronchial epithelia of xenografts with E1-deleted adenoviruses," Nature Genetics, 4, 27-34 (1993)
	FUJISAWA PHARMACEUTICAL CO., LTD., "Benzodiazepine derivatives," SciFinder Scholar, 2-3 (2002)
	GARCIA-ECHEVERRIA, C., "A Base Labile Handle for Solid Phase Organic Chemistry", Tetrahedron Letters, 38,52, 8933-8934 (1997)
	GRANT, R. et al., Grant and Hackh's Chemical Dictionary, McGraw-Hill Book Company, 282 (1987)

Examiner	Date	
Signature	Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Patent and Trademark Office: U.S. DEPARTMENT OF COMMERCE
Under the Paperwork Reduction Act of 1995, no persons are required to respond to a collection of information unless it contains a valid OMB number.

Substitute for form 1449B/PTO				Complete if Known		
2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2 2				Application Number	10/602,521	
<b>INFOR</b>	MATION	N DISCL	OSURE	Filing Date	June 24, 2003	
STATEMENT BY APPLICANT				First Named Inventor	David Edwin Thurston	
				Group Art Unit	1639	
(use as many sheets as necessary)			1	Examiner Name	Epperson, Jon D.	
Sheet	3	of	6	Attorney Docket Number	065435-9027	

	OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS				
Examiner Initials	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, pages(s), volume-issue numbers(s), publisher, city and/or country where published.				
	GREENE, T.W. and WUTS, P.G.M., Protective Groups in Organic Synthesis, John Wiley & Sons, 2 <sup>nd</sup> ed., Ch 7, 315-345 (1991)				
	GREGSON, S.J. et al., "Design, Synthesis and Evaluation of a Novel Pyrrolobenzodiazepine DNA-Interactive Agent with Highly Efficient Cross-Linking Ability and Potent Cytotoxicity", J. Med. Chem., 44: 737-748 (2001)				
	GREGSON, S.J. et al., "Effect of C2-exo Unsaturation on the Cytotoxicity and DNA-Binding Reactivity of Pyrrolo[2,1-c]1,4]benzodiazepines", Bioorganic & Medicinal Chemistry Letters, 10: 1845-1847 (2000)				
	HAUSKE, J. R. and DORFF, P., "Solid Phase CBZ Chloride Equivalent. A New Matrix Specific Linker", Tetrahedron Letters, 36, 10, 1589-1592 (1995)				
	HOCART et al., "Highly potent cyclic disulfide antagonists of somatostatin," J. of Medicinal Chem., 42:11 (1999)				
	HOLMES, C.P. and JONES, D.G., "Reagents for Combinatorial Organic Synthesis: Development of a New O-Nitrobenzyl Photolabile Linker for Solid Phase Synthesis", J. Org. Chem., 60, 2318-2319 (1995)				
	HUBER, B. et al., "Retroviral-mediated gene therapy for the treatment of hepatocellular carcinoma: An innovative approach for cancer therapy," <i>Proc. Natl. Acad. Sci. USA</i> , 88, 8039-8043 (1991)				
	JUNGHEIM, L.N. and SHEPHERD, T.A., "Design of Antitumor Prodrugs: Substrates for Antibody Targeted Enzymes," Am. Chem. Soc. Chem. Rev., 94, 1553-1566 (1994)				
	KAMAL, A., et al., "An Efficient Synthesis of Pyrrolo[2,1-c][1,4] Benzodiazepine Antibiotics via Reductive Cyclization," <i>Bioorg. Med. Chem. Ltrs</i> , 7, No. 14, 1825-1828 (1997)				

Examiner	Date
Signature	Considered

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute for form 1449B/PTO				Complete if Known		
				Application Number	10/602,521	
INFORMATION DISCLOSURE STATEMENT BY APPLICANT				Filing Date	June 24, 2003	
				First Named Inventor	David Edwin Thurston	
				Group Art Unit	1639	
(use as many sheets as necessary)			l	Examiner Name	Epperson, Jon D.	
Sheet	4	of	6	Attorney Docket Number	065435-9027	

	OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS
Examiner Initials	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, pages(s), volume-issue numbers(s), publisher, city and/or country where published.
	KAMAL, A., et al., "Synthesis of Pyrrolo [2,1-c][1,4]-Benzodiazepene Antibiotics: Oxidation of Cyclic Secondary Amine with TPAP", <i>Tetrahedron</i> , v. 53, No. 9, 3223-3230 (1997)
	KAPOOR, T.M. et al., "Exploring the Specificity Pockets of Two Homologous SH3 Domains Using Structure-Based, Split-Pool Synthesis and Affinity-Based Selection," J. Am. Chem. Soc. 120:23-29 (1998)
	KATRITZKY et al., Heterocyclic Chemistry, John Wiley & Sons, Inc., 247-253 (1960)
	KENNEDY, J.C. and POTTIER, R.H., "Endogenous protoporphyrin IX, a clinical useful photosensitiser for photodynamic therapy," J. Photochem Photobiol, 14, 275-292 (1992)
	KUNZ, H. and DOMBO, B., "Solid Phase Synthesis of Peptide and Glycopeptides on Polymeric Supports with Allylic Anchor Groups," <i>Angew Chem. Int. Ed. Engl</i> , 5, 711-713 (1988)
	KUZMICH, S. et al., "Increased levels of glutathione S-transferase $\pi$ transcript as a mechanism of resistance to ethacrynic acid," <i>Journal of Biochemistry</i> , 281, 219-224 (1992)
	LEIMGRUBER, W. et al., "Total synthesis of anthramycin," J. Am. Chem. Soc., 90, 5641-5643 (1968)
	LEWIS A.D. et al., "Glutathione and glutathione-dependent enzymes in ovarian adenocarcinoma cell lines derived from a patient before and after the onset of drug resistance: intrinsic differences and cell cycle effects," Carcinogenesis, 9, 1283-1287 (1988)
	MIZUSHIMA, S. and NAGATA, S., "pEF-BOS, a powerful mammalian expression vector," <i>Nucl. Acids Res.</i> , 18, 5322 (1990)

Examiner	Date	
Signature	Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute for form 1449B/PTO				Complete if Known		
				Application Number	10/602,521	
INFOR	MATION	DISCL	OSURE	Filing Date	June 24, 2003	
STATEMENT BY APPLICANT				First Named Inventor David Edwin Thurston		
				Group Art Unit	1639	
(use as many sheets as necessary)			•	Examiner Name	Epperson, Jon D.	
Sheet 5 of 6			6	Attorney Docket Number	065435-9027	

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS
Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, pages(s), volume-issue numbers(s), publisher, city and/or country where published.
MORGAN, R.A. and ANDERSON, W.F., "Human Gene Therapy," Annu. Rev. Biochem., 62, 191-217 (1993)
MOSMANN, T., "Rapid Colorimetric Assay for Cellular Growth and Survival: Application to Proliferation and Cytotoxicity Assays," J. Immunological Methods, 65, 55-63 (1983)
MULLEN, D.G. and BARANY, G., "A New Fluoridolyzable Anchoring Linkage for Orthogonal Solid-Phase Peptide Synthesis: Design, Preparation, and Application of the N-(3 or 4)-[[4-(Hydroxymethyl) phenoxy]-tert-butylphenylsilyl]phenyl Pentanedioic Acid Monoamide (Pbs) Handle", J. Org. Chem., 53, 5240-5248 (1988)
NICOLAOU, K.C. et al., "Designed Enediynes: A New Class of DNA-Cleaving Molecules with Potent and Selective Anticancer Activity," <i>Science</i> , 256, 1172-1178 (1992)
O'NEIL, I.A., et al., "The Synthesis of Functionalized Pyrrolo-[2,1-c][1,4]-Benzodiazepines," Synlett, 75-78 (1997)
PILLAI, V.N.R., "Photoremovable protecting groups in organic chemistry," Synthesis, 1-26 (1980)
RAM, Z. et al., "In Situ Retroviral-mediated Gene Transfer for the Treatment of Brain Tumors in Rats," Cancer Research, 53, 83-88 (1993)
REGULA, J. et al., "Photosensitisation and photodynamic therapy of oesophagael, duodenal and colorectal tumours using 5-aminoleavulic acid induced photoporphyrin IX-a pilot study," Gut, 36, 67-75 (1995)
SAGNOU, M.J. et al., "Design and Synthesis of Novel Pyrrolobenzodiazepine (PDB) Prodrugs for ADEPT and GDEPT," Bioorganic & Medicinal Chemistry Letters, 10, 2083-2086 (2000)

Examiner	Date	
Signature	Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute for form 1449B/PTO		Complete if Known			
				Application Number	10/602,521
INFORMATION DISCLOSURE			OSURE	Filing Date	June 24, 2003
STATEMENT BY APPLICANT			<b>ICANT</b>	First Named Inventor	David Edwin Thurston
		Group Art Unit	1639		
(use as many sheets as necessary)			•	Examiner Name	Epperson, Jon D.
Sheet	6	of	6	Attorney Docket Number	065435-9027

	OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS
Examiner Initials	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, pages(s), volume-issue numbers(s), publisher, city and/or country where published.
	SATYAM, A. et al., "Design, Synthesis, and Evaluation of Latent Alkylating Agents Activated by Glutathione S-Transferase," J. Med. Chem., 39, 1736-1747 (1996)
	SHIMIZU, K et al., "Prothracarcin, a Novel Antitumor Antibiotic," J. Antibiotics, 35, 972-978 (1982)
	STAR, W.M., "Light delivery and light dosimetry for photodynamic therapy," Lasers in Medical Science, 5:107-113 (1990)
	SUGGS, J.W. et al., "Synthesis and structure of anthramycin analogs via hydride reduction of dilactams," Tetrahedron Letters, 26, No. 40, 4871-4874 (1985)
	TEW, K.D. and CLAPPER, M.L., "Glutathione-S-transferase and anti-cancer drug resistance," <i>Mechanism of Drug Resistance in Neoplastic Cells</i> , Woolley, P.V. and Tew, K.D., Eds, Academic Press: Sand Diego, CA 141-159 (1988)
	THURSTON, D.E. et al., "Synthesis of Sequence-selective C8-linked Pyrrolo [2,1-c][1,4] Benzodiazepine DNA Interstrand Cross-linking Agent," J. Org. Chem., 61:8141-8147 (1996)
	UMEZAWA, H. et al., "Mazethramycins," SciFinder Scholar, 2-3 (2002)
	WILSON, S.C. et al., "Design, Synthesis, and Evaluation of a Novel Sequence-Selective Epoxide-Containing DNA Cross-Linking Agent Based on the Pyrrolo[2,1-c][1,4]benzodiazepine System", J. Med. Chem. 42:4028-4041 (1999)
	Dictionary of Science and Technology, Professor P.M.B. Walker ed. Larousse plc., pp. 63, 457, 523 (1995)

Examiner	Date	
Signature	Considered	

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.